UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/426,340	10/25/99	SANDAL T	5600.200-US

HM12/0616

STEVE T ZELSON ESQ
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE
SUITE 6400
NEW YORK NY 10174-6400

EXAMINER	
JOHANNSEN,D	
ART UNIT	**PAPER NUMBER**
1655	7
DATE MAILED:	06/16/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/426,340	Sandal et al
Examiner	**Group Art Unit**
Diana Johannsen	1655

☒ Responsive to communication(s) filed on *Mar 31, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-27* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5, 6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Objections

1. Claims 16 and 26-27 are objected to because of the following informalities. In claims 16 and 27, the phrase "an galactanase" should be amended to recite "a galactanase". In claim 26, the phrase "DNA encoding an polypeptide" should be amended to recite "DNA encoding a polypeptide". Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-27 are indefinite over the recitation of the terms "environmental pool of organisms" and "enriched environmental pool of organisms". It is unclear as to what is encompassed by this terminology. The specification states that "the term 'an environmental pool of organisms' means a environmental sample comprising microorganisms and cells from higher animals harboring DNA encoding a polypeptide with an activity of interest" (p. 3). However, the

specification cites examples of environmental samples that might or might not contain "cells from higher animals" (e.g., soil, plant material, sea or lake water). Accordingly, it is unclear as to what types of pools/samples would be embraced by the term "environmental pool", and as to how this claim language may further limit what one of skill in the art would consider to be an "environmental pool of organisms" (i.e., any sample comprising organisms obtained from an "environment"). Further, with respect to the term "enriched environmental pool" in claim 25, it is unclear as to how an "environmental pool of organisms enriched in DNA encoding a polypeptide with an activity of interest" would differ from an "enriched environmental pool of organisms enriched in DNA encoding a polypeptide with an activity of interest". The claims should be amended so as to clarify what types of pools of organisms are encompassed by the claims.

Claims 1-24 are indefinite over the recitation of the phrase "subjecting the environmental pool of organisms to cultivation in a medium and/or under conditions suitable for enriching said pool of organisms in organisms harbouring said DNA" in claims 1 and 21. First, it is unclear as to whether the limitation "suitable for enriching said pool of organisms..." is intended to refer to both the "medium" and the "conditions", or only to the "conditions". Accordingly, it is unclear as to whether the claimed methods require growth conditions "suitable for enriching said pool of organisms...", or whether the claims merely require "cultivation in a medium". Second, the language "conditions suitable for enriching said pool of organisms in organisms harbouring said DNA" is vague and indefinite. It is unclear whether this language requires growth conditions that

actually result in enrichment, or whether the claims merely require growth in conditions in which enrichment might occur. Accordingly, the metes and bounds of the claims are unclear.

Claims 1-24 are indefinite over the recitation of the limitation "the resulting enriched pool of organisms" in claims 1 and 21. There is insufficient antecedent basis for this limitation in the claims, as claims 1 and 21 do not previously refer to or recite a "resulting enriched pool of organisms".

Claims 2-4 are indefinite because it is unclear as to how the claims are intended to further limit claim 1, from which they depend. Claim 1 requires a step of "subjecting the environmental pool of organisms to cultivation in a medium and/or under conditions suitable for enriching said pool of organisms in organisms harbouring said DNA". Accordingly, the claim requires only cultivation "in a medium" OR "under conditions suitable....". Thus, with respect to claim 2 and dependent claims, which further limit "the medium" of claim 1, it is unclear as to how the claims further limit claim 1 as claim 1 may be limited to cultivation "under conditions suitable for enriching...". Clarification is required.

Claims 2-4 are indefinite over the recitation of the limitation "the gene product" in claim 2. There is insufficient antecedent basis for this limitation in the claims, as claim 1, from which claim 2 depends, does not recite a "gene product".

Claims 5-6 are indefinite over the recitation of the limitation "the enrichment" in claim 5. There is insufficient antecedent basis for this limitation in the claims, as claim 1, from which claim

5 depends, does not recite or refer to an "enrichment". It is also noted that claim 1 as currently written does not require a method step in which "enrichment" occurs.

Claim 6 is indefinite over the recitation of the limitation "the growth conditions". There is insufficient antecedent basis for this limitation in the claims, as claims 1 and 5, from which claim 6 depends, do not recite or refer to "growth conditions".

Claim 7 is indefinite over the recitation of the limitation "the growth conditions". There is insufficient antecedent basis for this limitation in the claim, as claim 1, from which claim 7 depends, does not recite or refer to "growth conditions". It is also noted that claim 1 as currently written does not require a method step in which "enrichment" occurs.

Claims 9-12 are indefinite over the recitation of the limitation "the pool of microorganisms" in claims 9-10 and 12. There is insufficient antecedent basis for this limitation in the claims, as claim 8, from which the claims, does not refer to or recite a "pool of microorganisms".

Claim 12 is indefinite because it is unclear as to how it is intended to further limit the claims from which it depends. The claim is drawn to "The method of claim 8, wherein the pool of microorganisms is enriched by supplying feed to the animal or insect". The claim does not make clear when this method step occurs in relation to the methods steps recited in claim 1, and as to how the step of enriching "by supplying feed" may relate to the "cultivation" step (step a)) of claim 1. The claim should be amended so as to clarify how it relates back to the claims from which it depends.

Claims 13-16 are indefinite over the recitation of the limitation "the gene libraries" in claim 13. There is insufficient antecedent basis for this limitation in the claims, as claim 1, from which claim 13 depends, recites the term "a gene library" but does not refer to or recite the term "gene libraries".

Claims 14-16 are indefinite over the recitation of the limitation "the enzyme of interest". There is insufficient antecedent basis for this limitation in the claims, as claims 1 and 13, from which the claims depend, do not refer to or recite an "enzyme of interest".

Claim 20 is indefinite over the recitation of the term "said organisms". It is unclear as to which "organisms" recited in claim 1 are indicated by this terminology (e.g., the "environmental pool of organisms" of step a), the "enriched pool of organisms" of step b)). Clarification is required.

Claims 21-24 are indefinite over the recitation of the phrases "method of selecting a DNA sequence of interest" and "selecting the DNA sequence of interest" in claim 21. It is unclear as to what is meant by the language "selecting a DNA sequence". For example, does this language require, e.g., detection of a sequence, isolation of a molecule, etc.? Further, it is unclear as to whether this language might encompass solely mental steps of "selecting" a sequence. Additionally, with respect to step d) of claim 21, it is unclear as to how a "DNA sequence of interest" would "result from the screening of step c)". The claims should be amended so as to provide a clear and definite descriptions of the objective and required final process step of the claimed method.

Claims 21-24 are indefinite over the recitation of the limitation "the desired gene" in claim 21. There is insufficient antecedent basis for this limitation in the claims, as claim 21 does not previously refer to or recite a "desired gene".

Claims 22-23 are indefinite over the recitation of the limitation "the gene library" in each of the claims. There is insufficient antecedent basis for this limitation in the claims, as claims 21, from which claims 22-23 depend, does not recite a "gene library".

Claim 23 is indefinite because it is unclear as to how it is intended to further limit claim 21, from which it depends. Specifically, it is unclear as to how the step of screening "for enzymes under conditions which the enzyme is active [sic]" relates to and further limits the method steps recited in claim 21. For example, is this step to be performed in addition to the steps of claim 21, or is this language intended to modify one of the steps recited in claim 21? Clarification is required.

Claim 23 is indefinite over the recitation of the term "the enzyme". There is insufficient antecedent basis for this limitation in the claims, as neither claim 23 nor claim 21 previously recite an "enzyme".

Claim 24 is indefinite because it is unclear as to how it is intended to further limit claim 21. Specifically, it is unclear as to whether the step recited in claim 24 is intended to be performed in addition to the method steps of claim 21, or whether claim 24 is intended to further limit the "screening" step (step c)) of claim 21. Clarification is required.

Claims 25-27 are indefinite over the recitation of the phrase "A gene library prepared from an enriched environmental pool of organisms enriched in DNA encoding a polypeptide with an activity of interest" in claim 25. The claims are drawn to a product (a gene library), and it is unclear as to how the limitation "prepared from an enriched environmental pool of organisms enriched in DNA encoding a polypeptide with an activity of interest" is intended to limit the structural and/or functional properties of the library encompassed by the claims. The claims should be amended so as to provide a clear and definite description of the molecules encompassed thereby.

Claims 26-27 are indefinite over the recitation of the phrase "wherein the DNA encoding an [sic] polypeptide with an activity of interest comprises an enzyme, a hormone or a toxin" in claim 26. It is unclear as to whether Applicants' intent is to actual indicate that the recited DNA comprises a protein ("an enzyme, a hormone or a toxin"), or whether Applicants' intent is to indicate that recited DNA encodes an enzyme, a hormone or a toxin (i.e., that the encoded polypeptide is an enzyme, a hormone or a toxin). Clarification is required.

Claim 27 is indefinite over the recitation of the phrase "wherein the DNA is an enzyme which comprises....". It is unclear as to what is meant by this language, as this language suggests that the recited DNA is a protein. Clarification is required.

Claim Rejections - 35 U.S.C. § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3, 5-6, 13-15, 17-23, and 25-26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Duvick et al (WO 96/06175 [2/1996]).

Duvick et al teach methods for identifying organisms having a particular enzymatic activity (fumonisin degradation) by growing the organisms in media in which the enzyme substrate (fumonisin B1 or B2) is provided as the sole carbon source (p. 4-6, Example 1). The organisms employed in Duvick et al's methods are from "environmental pools" (e.g., seeds and stalks [see p. 4]). Duvick et al teach genomic libraries and disclose methods for preparing said genomic libraries from the nucleic acids of the microorganisms encoding the protein of interest (a fumonisin esterase) (p. 24-25). Furthermore, Duvick et al discloses screening libraries for genes encoding proteins having the ability to degrade a particular substrate (fumonisin), and disclose "selecting" such genes for further analysis (subcloning, sequencing, expression, etc.) (p. 25). Accordingly, Duvick et al clearly anticipate the instant claims. With further reference to claim 6, it is noted that it is an inherent property of the growth conditions employed by Duvick et al (or of any growth conditions) that they "comprise pH and temperature". With respect to claims 14-15, it is noted that the "enzyme of interest" taught by Duvick et al is an esterase (see, e.g., p. 18-23).

With respect to claim 19, it is noted that Duvick et al teach both fungal and bacterial pools of organisms (p. 4). With respect to claim 20, Duvick et al discloses cultures of organisms that are enriched with respect to fumonisin degradation (see, e.g., p. 4). With respect to claim 23, it is noted that Duvick et al disclose screening clones for "their ability to degrade fumonisin" and selection of "colonies that degrade fumonisin" (p. 25).

Claim Rejections - 35 U.S.C. § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 4, 7, 16, 24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al (WO 96/06175 [2/1996]) in view of Sarkar and Upadhyay (Folia Microbiologica 38(1):29-32 [1993]).

Duvick et al teach methods for identifying organisms having a particular enzymatic activity (fumonisin degradation) by growing the organisms in media in which the enzyme substrate (fumonisin B1 or B2) is provided as the sole carbon source (p. 4-6, Example 1). The organisms employed in Duvick et al's methods are from "environmental pools" (e.g., seeds and stalks [see p. 4]). Duvick et al teach genomic libraries and disclose methods for preparing said genomic libraries from the nucleic acids of the microorganisms encoding the protein of interest (a

fumonisin esterase) (p. 24-25). Furthermore, Duvick et al discloses screening libraries for genes encoding proteins having the ability to degrade a particular substrate (fumonisin), and disclose "selecting" such genes for further analysis (subcloning, sequencing, expression, etc.) (p. 25). Duvick et al do not teach employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide "with an activity of interest" that acts on the substrates set forth in claim 4, and/or nucleic acids encoding enzymes of the types set forth in claims 16 or 27. Further, Duvick et al do not teach or suggest "selecting" genes encoding such polypeptides, as required by claim 24. Finally, Duvick et al do not teach or suggest employing growth conditions such as those set forth in claim 7.

Sarkar and Upadhyay disclose that *Bacillus thermoalcaliphilus* isolated from an environmental sample ("the soil of a termite") produces a cellulase that is most stable at pH 8.5-9.5 and optimally active at 70°C (see entire reference, especially p. 29-30). Further, Sarkar and Upadhyay teach growth of this bacterium in media comprising cellulose at 60°C, pH 8.5 (p. 29). In view of the teachings of Sarkar and Upadhyay, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Duvick et al so as to have employed Duvick et al's methods to prepare a genomic library enriched for a gene encoding the thermostable cellulase taught by Sarkar and Upadhyay, and so as to have "selected" that gene for further analysis. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing the cellulase-encoding gene, rapidly preparing recombinant forms of the cellulase for additional study, etc.

With respect to claim 4, it is further noted that Sarkar and Upadhyay disclose that cellulose is a substrate for cellulase, and teach growth of cellulase producing organisms in media comprising cellulose. With respect to claim 7, it is further noted that it would have been *prima facie* obvious to one of ordinary skill in the art to have selected the growth conditions taught by Sarkar and Upadhyay in order to assure optimal growth of the bacterium from which nucleic acids of interest were to be cloned, for the advantages of convenience and efficiency.

8. Claims 4, 8-9, 16, 24, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al in view of Cotta (Appl. Environment. Microbiol. 54(3):772-776 [3/1988]).

The teachings of Duvick et al are set forth in paragraph 7, above. Duvick et al do not teach or suggest employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide of interest from an environmental pool "isolated from an animal stomach or an insect gut", as required by claim 8, or from a pool of microorganisms "isolated from a cow's rumen", as required by claim 9. Further, Duvick et al do not teach employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide "with an activity of interest" that acts on the substrates set forth in claim 4, and/or nucleic acids encoding enzymes of the types set forth in claims 16 or 27. Additionally, Duvick et al do not teach or suggest "selecting" genes encoding such polypeptides, as required by claim 24.

Cotta teaches that several bacteria present in the rumen of cattle produce amylases that degrade starch (see entire reference). In view of the teachings of Cotta, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have

modified the invention of Duvick et al so as to have employed Duvick et al's methods to prepare genomic libraries enriched for genes encoding the amylases taught by Cotta, and so as to have "selected" such genes for further analysis. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing the amylase-encoding genes, rapidly preparing recombinant forms of the amylases for additional study, etc. With respect to claim 4, it is noted that Cotta teaches that amylases degrade amylose (see, e.g., p. 773).

9. Claims 4, 8, 10, 12, 16, 24, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al in view of Jacobsen and Schlein (J. Euk. Microbiol. 44(3):216-219 [1997]).

The teachings of Duvick et al are set forth in paragraph 7, above. Duvick et al do not teach or suggest employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide of interest from an environmental pool "isolated from an animal stomach or an insect gut", as required by claim 8, or from "the gut of an insect of the Isoptera, Lepidoptera, Coleoptera, or Diptera families", as required by claim 10. Further, Duvick et al do not teach employing their methods to prepare libraries enriched in nucleic acids encoding a polypeptide "with an activity of interest" that acts on the substrates set forth in claim 4, and/or nucleic acids encoding enzymes of the types set forth in claims 16 or 27. With respect to claim 12, Duvick et al do not teach or suggest supplying a substrate in the feed of an animal or insect. Additionally,

Duvick et al do not teach or suggest "selecting" genes encoding such polypeptides, as required by claim 24.

Jacobsen and Schlein teach that *Leishmania* present in the midgut of the sandfly *Phlebotomus papatasi* produce cellulases that degrade cellulose (see entire reference). In view of the teachings of Jacobsen and Schlein, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Duvick et al so as to have employed Duvick et al's methods to prepare genomic libraries enriched for genes encoding the cellulases taught by Jacobsen and Schlein and so as to have "selected" such genes for further analysis. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing the cellulase-encoding genes, rapidly preparing recombinant forms of the cellulases for additional study, etc. With respect to claim 4, it is noted that Jacobsen and Schlein teaches that cellulases degrade cellulose (see, e.g., p. 216). With respect to claim 10, it is noted that *Phlebotomus papatasi* is a member of the order Diptera. With respect to claim 12, it is noted that Jacobsen and Schlein suggest feeding flys with feed that comprises cellulose (p. 216).

10. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duvick et al in view of Jacobsen and Schlein, as applied to claims 4, 8, 10, 12, 16, 24 and 27, above, and further in view of Siegle et al (US Patent No.4,027,037).

The combined references of Duvick et al and Jacobsen and Schlein do not teach or suggest preparing "enriched" gene libraries from microorganisms isolated from the guts of the insect

species set forth in claim 11. It is noted that the instant claim is not limited to methods in which, e.g., a gene encoding a polypeptide having a particular activity in a particular species is identified or detected. Accordingly, the instant claim encompasses methods of preparing a library comprising any DNA "encoding a polypeptide with an activity of interest" from any pool of microorganisms isolated from the gut of any of the species set forth in the claim. Siegle et al teach a variety of orders and species of arthropods, including both *Phlebotomus* species and *Agrotis* species (col 6, line 32-col 7, line 38). In view of the teachings of Siegle et al, it would have been *prima facie* obvious at the time the invention was made to have modified the method of Duvick et al in view of Jacobsen and Schlein so as to have prepared enriched gene libraries from nucleic acids of the gut bacteria of any of the arthropods taught by Siegle et al, including *Agrotis* species. An ordinary artisan would have been motivated to have made such a modification for the advantage of, e.g., rapidly isolating and sequencing a gene encoding any polypeptide of interest, rapidly preparing recombinant forms such a polypeptide for additional study, etc.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday from 7:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at 703/308-1152. The fax phone number for the

Technology Center where this application or proceeding is assigned is 703/305-3014 or 305-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana Johannsen

June 14, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

6/14/00